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EDITORIAL

Hyaline arteriolosclerosis: New meaning for an old lesion

Hyaline arteriolosclerosis is a common vascular lesion characterized by the accumulation of various serum proteins in the subendothelial space often extending into the media. Hyalin has a characteristic morphologic appearance, staining bright magenta with periodic acid-Schiff (PAS) stain and having a glassy texture. This lesion is seen in many different situations, including aging, hypertension, diabetes mellitus, and focal segmental glomerulosclerosis (FSGS). Moritz and Oldt [1] first described the frequent occurrence of hyaline arteriolosclerosis with increasing age. He also noted that hypertension increased the frequency of hyaline arteriolosclerosis more in the kidney than in other organs. Hyaline arteriolosclerosis is one component of the constellation of findings seen in diabetic nephropathy. The lesion is also seen in FSGS to a greater extent than in other renal diseases affecting glomeruli such as immunoglobulin A (IgA) nephropathy [2].

Previous studies have suggested that hyaline arteriolosclerosis is associated with impaired autoregulation. Autoregulation is the process that allows the kidney to maintain a constant blood flow and glomerular filtration rate (GFR) at mean blood pressure that varies between 80 and 160 mm Hg [3]. This response is mediated by an as yet imperfectly understood combination of myogenic reflexes and tubuloglomerular feedback. Little is known about the effects of aging on autoregulation. In early hypertension, the autoregulatory curve is shifted to the right so that renal blood flow and GFR remain stable at higher than normal blood pressures [3]. It has been suggested, however, that autoregulation is impaired when long-standing hypertension is accompanied by hyaline arteriolosclerosis [3]. One consequence of this loss of autoregulation may be transmission of increased systemic pressure to the glomerulus. A similar picture is seen in patients with diabetic nephropathy. Christensen and Parving [4] found that diabetic patients with hypertension and nephropathy had diminished autoregulatory capacity. Four of the 14 patients tested had a completely pressure-passive vasculature. In these patients, the preglomerular vessels appeared not to respond to changes in mean arterial pressure so that peaks in systemic pressure could be transmitted to the glomeruli, increasing the risk of glomerular injury. Impaired autoregulation has also been described in a variety of glomerulopathies associated with proteinuria, including one case of FSGS [5].

Key words: hyaline arteriolosclerosis, autoregulation, aging kidney.

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In this issue of *Kidney International*, Hill and Bariety [6] examine the relationship between hyaline arteriolosclerosis and glomerular structure in aging humans. They identify three types of changes in the afferent arteriole (no hyalin, nonobstructing hyalin, or obstructing hyalin) and four glomerular types (normal, hypertrophic, segmental sclerosis, and ischemic). Hyalin is considered nonobstructing when it does not intrude into the vessel lumen. Hill and Bariety found that the afferent arterioles with nonobstructing hyaline deposits had increased lumen diameter and wall thickness as compared to the other two types of arterioles. Of note, the muscle layer was thinner in the areas of hyaline deposition, possibly impairing the ability of the vessel to constrict. Most of the glomeruli associated with these large arterioles had increased tuft size, dilated hilar capillaries, increased mean area of individual capillaries, and increased total capillary area.

As recognized by Hill and Bariety, the finding of an association between hyalin and increased arteriolar size does not establish the cause of hyaline deposition. One possible explanation is that increased wall tension triggers injury in enlarged vessels. Hill and Bariety [6] suggest that whatever the mechanism of its formation, the presence of hyalin is associated with impaired autoregulation. They propose that autoregulation is lost in those individual nephron units in the aging kidney with an enlarged arteriole and its accompanying large glomerulus. Local loss of autoregulation, of course, cannot be proved in pathologic material alone. However, experimental studies using the renal ablation model suggest that nephron enlargement is accompanied by loss of autoregulation [7, 8]. Impaired autoregulation has also been recognized in a model of FSGS, the fawn-hooded rat [9]. An interesting unanswered question is whether hyalin in arterial walls contributes to loss of autoregulation or whether hyalin is deposited only after autoregulation becomes impaired.

What can be gained by paying new attention to this old lesion, hyaline arteriolosclerosis? Does hyaline arteriolosclerosis make a difference? We know that this lesion is seen with glomerulosclerosis. Does its presence accelerate glomerulosclerosis so that we might be able to use it to predict the later occurrence of glomerular scarring? The extent of hyaline arteriolosclerosis has been associated with prognosis in FSGS [10]. It could be that interfering with the development of hyaline arteriolosclerosis could provide another avenue for therapeutic intervention in the war on progression of renal disease.

An immediately practical question also arises. What does the possible association between hyaline arteriolosclerosis and loss of autoregulation tell us about the use of aging kidneys in transplantation? If hyaline arteriolosclerosis is a marker for loss of autoregulation, then it may predict the loss of additional glomeruli in a single kidney. Finally, we should congratulate Hill and Bariety for reminding us that we need to look at vessels as well as at glomeruli. After all, renal pathologists teach medical students, pathology residents, nephrology fellows, and nephrologists that we must examine all the compartments of the kidney in our analysis of the renal biopsy. Likewise, in our research, we must consider the whole kidney and the interactions of the four compartments if we are to understand the pathophysiology of renal disease.

Jean L. Olson
San Francisco, California

Correspondence to Jean L. Olson, M.D., Professor of Clinical Pathology, Department of Pathology, S-568A, University of California San Francisco, 505 Parnassus Avenue, San Francisco, CA 94143, USA.
E-mail: jolson@itsa.ucsf.edu

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